

Attorney Docket No. 50623.349

**CLAIM AMENDMENTS**

In this Final Claim Amendments, Applicants have amended Claims 19, 21, 22, 28, 32, 39, 50 and 54 and submitted New Claims 61-67.

Claims 1-11 (canceled).

12. (previously presented) A method of delivering a drug through a membrane junction or a cell membrane comprising:

delivering a permeabilizing reagent to a membrane junction or a cell membrane in a concentration sufficient to increase the permeability of the membrane junction or cell membrane; and

delivering a drug to the membrane junction or cell membrane, wherein the drug travels through the membrane junction or cell membrane.

13. (original) The method of Claim 12, wherein the permeabilizing reagent is delivered by a stent and/or a catheter.

14. (original) The method of Claim 12, wherein the drug is delivered by a stent and/or a catheter.

15. (original) The method of Claim 12, wherein the permeabilizing reagent is a solution including a solute selected from the group consisting of glucose, mannose, maltose, dextrose, fructose, sodium chloride, sodium citrate, sodium phosphate, polyethylene glycol, polyvinyl pyrrolidone and amino acids.

16. (original) The method of Claim 12, wherein the permeabilizing reagent is selected from the group consisting of iminodiacetic acid, nitriloacetic acid, ethylenediaminomonoacetic acid, ethylenediaminodiacetic acid, ethylenediaminotetraacetic acid, sodium taurodihydrofusidate, sodium salicylate, sodium caprate, sodium glycocholate,

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cholylsarcosine, isopropyl myristate, partially hydrolyzed triglycerides, fatty-acid sugar derivatives, oleic acid derivatives, histamine, bradykinin and its conformational analogs, tumor necrosis factor alpha, nitroglycerine, sodium nitroprusside, diethylamine sodium, 3-morpholinositydnonimine, S-nitroso-N-acetyl-penicillamine, and vascular endothelial growth factor and combinations thereof.

Claims 17 and 18 (canceled).

19. (currently amended) A method of local drug delivery, comprising:

locally applying a permeabilizing reagent to a selected area of a body tissue to increase the permeability of a cellular barrier; and

locally applying a drug to the body tissue.

20. (original) The method of Claim 19, wherein the permeabilizing reagent is applied before or concomitantly with the drug.

21. (currently amended) The method of Claim 19, wherein the local application of the permeabilizing reagent and the drug isare via a stent.

22. (currently amended) The method of Claim 19, wherein the permeabilizing reagent is selected from the group consisting of a hyperosmotic solution, a calcium ion chelator, a surfactant, and a receptor-mediated permeabilizing reagent.

23. (previously presented) The method of Claim 19, additionally including applying a P-glycoprotein system blocker.

24. (previously presented) The method of Claim 23, wherein the application of the P-glycoprotein system blocker follows application of the permeabilizing reagent.

25. (previously presented) The method of Claim 23, wherein the P-glycoprotein system blocker is selected from the group consisting of Pluronic P-85®, verapamil, disulfiram

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and antisense oligonucleotide complementary to a messenger RNA encoding P-glycoprotein and combinations thereof.

26. (previously presented) The method of Claim 19, wherein the drug is selected from the group consisting of antineoplastic, antimitotic, antiinflammatory, antiplatelet, antiallergic, anticoagulant, antifibrin, antithrombin, antiproliferative, antioxidant, antimigratory, antiextracellular matrix deposition, pro-apoptotic, nitric oxide donor, pro-angiogenic, and pro-arteriogenic substances and combinations thereof.

27. (previously presented) A method of delivering a drug through a membrane junction or a cell membrane comprising:

delivering a hyperosmotic solution, a calcium ion chelator, a surfactant, and/or a receptor-mediated permeabilizing reagent to a membrane junction or a cell membrane in a concentration sufficient to increase the permeability of the membrane junction or cell membrane; and

delivering a drug to the membrane junction or cell membrane, wherein the drug travels through the membrane junction or cell membrane.

28. (currently amended) A method of local drug delivery, comprising:

(a) locally applying a hyperosmotic solution, a calcium ion chelator, a surfactant, and/or a receptor-mediated permeabilizing reagent to a selected area of a body tissue to increase the permeability of a cellular barrier; and

(b) locally applying a drug to the body tissue.

29. (previously presented) A method of local drug delivery, comprising:

locally applying a P-glycoprotein system blocker to a selected area of a body tissue; and  
locally applying a drug to the body tissue.

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30. (previously presented) The method of Claim 29, further comprising locally applying a permeabilizing reagent to the body tissue.

31. (previously presented) The method of Claim 30, wherein the permeabilizing reagent is applied before the P-glycoprotein system blocker.

32. (currently amended) The method of Claim 30, wherein the permeabilizing reagent is selected from the group consisting of ~~an osmotic agent~~ a hyperosmotic solution, a calcium ion chelator, a surfactant, and a receptor-mediated permeabilizing reagent.

33. (previously presented) The method of Claim 29, wherein the P-glycoprotein system blocker is selected from the group consisting of Pluronic P-85®, verapamil, disulfiram and antisense oligonucleotide complementary to a messenger RNA encoding P-glycoprotein and combinations thereof.

34. (previously presented) The method of Claim 29, wherein the P-glycoprotein system blocker or the drug is carried by a stent.

35. (previously presented) A method of delivering a drug through a membrane junction or a cell membrane comprising:

delivering a hyperosmotic solution to a membrane junction or a cell membrane in a concentration sufficient to increase the permeability of the membrane junction or cell membrane;  
and

delivering a drug to the membrane junction or cell membrane, wherein the drug travels through the membrane junction or cell membrane.

36. (previously presented) The method of Claim 35, wherein the hyperosmotic solution is delivered by a catheter.

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37. (previously presented) The method of Claim 35, wherein the drug is delivered by a stent and/or a catheter.

38. (previously presented) The method of Claim 35, wherein the hyperosmotic solution includes a solute selected from the group consisting of glucose, mannose, maltose, dextrose, fructose, sodium chloride, sodium citrate, sodium phosphate, polyethylene glycol, polyvinyl pyrrolidone and amino acids.

39. (currently amended) A method of local drug delivery, comprising:  
positioning a stent at a selected area of a body tissue, the stent carrying a permeabilizing reagent to increase the permeability of a cellular barrier; and  
locally applying a drug to the body tissue.

40. (previously presented) The method of Claim 39, wherein the permeabilizing reagent is selected from the group consisting of iminodiacetic acid, nitriloacetic acid, ethylenediaminomonoacetic acid, ethylenediaminodiacetic acid, ethylenediaminetetraacetic acid, sodium taurodihydrofusidate, sodium salicylate, sodium caprate, sodium glycocholate, cholylsarcosine, isopropyl myristate, partially hydrolyzed triglycerides, fatty-acid sugar derivatives, oleic acid derivatives, histamine, bradykinin and its conformational analogs, tumor necrosis factor alpha, nitroglycerine, sodium nitroprusside, diethylamine sodium, 3-morpholinosydnonimine, S-nitroso-N-acetyl-penicillamine, and vascular endothelial growth factor and combinations thereof.

41. (previously presented) The method of Claim 39, wherein the stent is positioned before or during the application of the drug.

42. (previously presented) The method of Claim 39, wherein the local application of the drug is via a stent.

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43. (previously presented) The method of Claim 39, wherein the permeabilizing reagent is selected from the group consisting of a calcium ion chelator, a surfactant, and a receptor-mediated permeabilizing reagent.

44. (previously presented) The method of Claim 39, wherein the stent additionally carries a P-glycoprotein system blocker.

45. (previously presented) The method of Claim 44, wherein the P-glycoprotein system blocker is selected from the group consisting of Pluronic P-85®, verapamil, disulfiram and antisense oligonucleotide complementary to a messenger RNA encoding P-glycoprotein and combinations thereof.

46. (previously presented) The method of Claim 39, wherein the drug is selected from the group consisting of antineoplastic, antimitotic, antiinflammatory, antiplatelet, antiallergic, anticoagulant, antifibrin, antithrombin, antiproliferative, antioxidant, antimigratory, antiextracellular matrix deposition, pro-apoptotic, nitric oxide donor, pro-angiogenic, and pro-arteriogenic substances and combinations thereof.

47. (previously presented) The method of Claim 39, wherein the permeabilizing reagent is carried by a polymeric coating on the stent.

48. (previously presented) The method of Claim 39, wherein the stent additionally carries the drug.

49. (previously presented) The method of Claim 48, wherein the stent carries the permeabilizing reagent and the drug in a coating, wherein the coating includes the permeabilizing reagent in a first layer and the drug in a second layer.

50. (currently amended) A method of local drug delivery, comprising:  
positioning a stent at a selected area of a body tissue, the stent carrying a drug; and

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locally applying a permeabilizing reagent to the body tissue to increase the permeability of a cellular barrier.

51. (previously presented) The method of Claim 50, wherein the permeabilizing reagent is selected from the group consisting of iminodiacetic acid, nitriloacetic acid, ethylenediaminomonoacetic acid, ethylenediaminodiacetic acid, ethylenediaminetetraacetic acid, sodium taurodihydrofusidate, sodium salicylate, sodium caprate, sodium glycocholate, cholylsarcosine, isopropyl myristate, partially hydrolyzed triglycerides, fatty-acid sugar derivatives, oleic acid derivatives, histamine, bradykinin and its conformational analogs, tumor necrosis factor alpha, nitroglycerine, sodium nitroprusside, diethylamine sodium, 3-morpholinosydnonimine, S-nitroso-N-acetyl-penicillamine, and vascular endothelial growth factor and combinations thereof.

52. (previously presented) The method of Claim 50, wherein the permeabilizing reagent is applied before or during positioning of the stent.

53. (previously presented) The method of Claim 50, wherein the local application of the permeabilizing reagent is via a stent.

54. (currently amended) The method of Claim 50, wherein the permeabilizing reagent is selected from the group consisting of a hyperosmotic solution, a calcium ion chelator, a surfactant, and a receptor-mediated permeabilizing reagent.

55. (previously presented) The method of Claim 50, wherein the stent additionally carries a P-glycoprotein system blocker.

56. (previously presented) The method of Claim 55, wherein the P-glycoprotein system blocker is selected from the group consisting of Pluronic P-85®, verapamil, disulfiram

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and antisense oligonucleotide complementary to a messenger RNA encoding P-glycoprotein and combinations thereof.

57. (previously presented) The method of Claim 50, wherein the drug is selected from the group consisting of antineoplastic, antimitotic, antiinflammatory, antiplatelet, antiallergic, anticoagulant, antifibrin, antithrombin, antiproliferative, antioxidant, antimigratory, antiextracellular matrix deposition, pro-apoptotic, nitric oxide donor, pro-angiogenic, and pro-arteriogenic substances and combinations thereof.

58. (previously presented) The method of Claim 50, wherein the drug is carried by a polymeric coating on the stent.

59. (previously presented) The method of Claim 50, wherein the stent additionally carries the permeabilizing reagent.

60. (previously presented) The method of Claim 59, wherein the stent carries the permeabilizing reagent and the drug in a coating, wherein the coating includes the permeabilizing reagent in a first layer and the drug in a second layer.

Please insert the following New Claims:

61. (new) The method of Claim 12, wherein the permeabilizing reagent is selected from the group consisting of a hyperosmotic solution, a calcium ion chelator, a surfactant, and a receptor-mediated permeabilizing reagent.

62. (new) The method of Claim 19, wherein the local application of the permeabilizing reagent is via a catheter and the local application of the drug is via a stent.

63. (new) The method of Claim 28, wherein steps (a) and (b) are performed via a stent.



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64. (new) The method of Claim 28, wherein step (a) is performed via a catheter and step (b) is performed via a stent.

65. (new) The method of Claim 29, wherein the local application of the P-glycoprotein system blocker and the local application of the drug are via a stent.

66. (new) The method of Claim 29, wherein the local application of the P-glycoprotein system blocker is via a catheter and the local application of the drug is via a stent.

67. (new) The method of Claim 50, wherein the permeabilizing reagent is a solution including a solute selected from the group consisting of glucose, mannose, maltose, dextrose, fructose, sodium chloride, sodium citrate, sodium phosphate, polyethylene glycol, polyvinyl pyrrolidone and amino acids.